

MDUFA III Implementation

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Hello . I am Barbara Zimmerman, the Deputy Director for Program Management of Operations in the Office of Device Evaluation. I am pleased to be here today to discuss the implementation of the third Medical Device User Fee Act. I will be referring to it as MDUFA III.

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In this presentation I am going to discuss:

- what FDA and Industry agreed to in the MDUFA III commitment letter and
- the status, as of today, Nov. 15, 2012, of implementing each section of the commitment letter.

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The enactment in 2002 of the Medical Device User Fee and Modernization Act was prompted by growing concerns about the medical device review program's capacity and performance. MDUFA I and MDUFA II, which was enacted in 2007, authorized user fees for the review of medical device premarket applications, reports, supplements, and premarket notification submissions.

These additional resources enabled FDA to make reviews more timely, predictable, and transparent to applicants. MDUFA fees and mandated appropriations for the medical device program helped FDA expand available expertise, modernize its information management systems, provide new review options, and provide more guidance to prospective applicants.

Today we will be discussing the MDUFAIII commitments. These commitments strike a careful balance between what industry agreed to pay and what FDA can accomplish with the additional funding.

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MDUFA III is authorized in Title II of the FDA Safety and Innovation Act (FDAuSIA). Included in the other Titles of FDAuSIA is the authorization for FDA to collect user fees from industry to fund reviews of innovator drugs, generic drugs and biosimilar biologics. In addition, there are many other provisions beyond the four user fee programs.

Such as:

- a new de novo pathway for low risk devices which do not have a predicate device,
- modifications to the Investigational Device Exemption program, and
- Modifications to the post-market surveillance study program.

The nonuser fee provisions of FDAuSIA became effective on July 9th, 2012. Where, the user fee provisions, including MDUFA III, did not go into effect until Oct. 1, 2012.

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FDA met with industry to negotiate final commitments of MDUFA III over a 13 month period, from January, 2011 through February 2012. This was a long 13 months.

In addition, when MDUFA II was reauthorized in 2007, Congress directed FDA to take additional steps to ensure that public stakeholders would have adequate opportunity to provide input into the program enhancements. Therefore, in addition to meeting with Industry, FDA met with public stakeholders monthly during the negotiation process.

Meeting minutes from FDA's meetings with Industry and Public Stakeholders are available on FDA's webpage.

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On March 15, 2012 FDA made public the package of proposed recommendations which included the agreed upon commitment letter by Industry and FDA.

The MDUFA III commitments address many of the priorities, concerns, and important challenges identified by:

- public stakeholders,
- the device industry, and
- FDA

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The MDUFA III commitment letter is the product of a successful negotiation process between Industry and FDA. MDUFA III authorizes FDA to collect 595 million dollars in user fees over 5 years. Some of the notable improvements to the MDUFA program include:

- FDA's facilitation of earlier, more transparent, and predictable interactions between FDA and Industry
- More rigorous premarket review performance goals, and
- Outcome goals which are shared by both Industry and FDA.

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I am now going to cover, in detail, the key features of the MDUFA III commitment letter.

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This slide lists the process and policy improvements I will be covering in the next several slides.

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The first process and policy improvement I am going to discuss is the improved pre-submission process.

The improved pre-submission process officially expands the pre-IDE program to all submission types and defines a pre-submission application more clearly.

The modified pre-submission process is articulated in the draft guidance "The pre-submission program and meetings with FDA staff". We are in the process of finalizing this guidance document based on the comments we received. Once finalized this guidance is intended to be used by both Industry and FDA to improve the predictability and consistency of the pre-submission process.

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With the new performance goals established in MDUFA III, acceptance review takes on additional importance in encouraging quality applications from Industry. The intent of a more rigorous acceptance review is to allow FDA reviewers to concentrate resources on complete applications.

The new Refuse To Accept criteria for 510(k) and PMA is a checklist of objective criteria for screening out submissions that lack basic requirements. In accordance with the MDUFA III commitments, if a submission is refused for acceptance, the review clock does not start until FDA receives a revised submission that meets the established acceptance criteria. This approach will provide a more efficient strategy for ensuring that safe and effective medical devices are cleared for marketing as quickly as possible.

Draft guidance documents have been issued for both the 510(k) and PMA Refuse To Accept policy.

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Next, I am going to explain the modified interactive review process. The modified process is intended to:

- Improve the interaction between the FDA review staff and the applicant during the review process
- Prevent unnecessary delays in the completion of the review
- Ensure that FDA's concerns are clearly communicated to the applicant and are appropriate; and
- Decrease the number of review cycles by minimizing the number of review questions conveyed through deficiency letters.

The existing interactive review guidance document is being revised to elaborate on the modified interactive review process as outlined in the MDUFA III commitment letter and will be issued in the near future. In the meantime, FDA has already begun implementing process and policy improvements which are consistent with the interactive review section of the commitment letter. I would like to take this opportunity to encourage all of industry to embrace the improved interactive review process. As stated in the commitment letter, Interactive review entails responsibilities for both FDA and applicants. It will be impossible for FDA and Industry to achieve the shared outcome goals if we do not work together to make interactive review a success.

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- The first item on this slide summarizes the new substantive interaction commitment. The purpose of substantive interactions is to communicate to the applicant if FDA will continue to resolve any outstanding deficiencies through an interactive review without placing the file on hold or if deficiencies have been identified which warrant placing the submission on hold. Substantive interaction occurs after the FDA has performed a complete review of the submission. It should be noted that the substantive interaction goal is a distinct milestone and should not be confused with interactive review.
- The next item on this slide highlights FDA's commitment to improving the process of developing, reviewing, tracking, issuing, and updating guidance documents as resources permit, but not to the detriment of meeting the quantitative review timelines and statutory obligations.

Specifically:

- the agency will review the guidance documents currently available on its website to determine if a guidance should either be deleted because it no longer represents the agency's current thinking, or the agency will place a notation on the guidance that the document is currently under review by the agency.
- It will provide an "A" list and a "B" list of guidance documents it intends to publish, and
- It will establish a process for stakeholders to have an opportunity to comment on these lists.
- The last item on this slide reinforces FDA's commitment to support the third party review process as well as strengthen and improve the program. In addition, FDA will publish criteria for re-accreditation of third party reviewers. Re-accreditation criteria are not included in the MDUFA III commitment letter but were included as a provision in FDAuSIA.

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As part of FDA's commitment to patient safety and risk tolerance, we have issued guidance on the "Factors to Consider When Making a Benefit-Risk Determination in Medical Device Premarket Applications and De Novo Classifications".

In addition, FDA committed to meet with patient groups to better understand patient perspectives and to provide patients' views early in the medical product development process.

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The first item on this slide outlines FDA's commitment to propose additional low risk medical devices to exempt from premarket notification. However, it should be noted that even though FDA has committed to providing a list of additional devices to exempt from premarket notification, FDAuSIA has incorporated new provisions to reclassify products. FDA is currently reviewing these new provisions and will continue to work toward exempting additional low risk medical devices as resources permit.

The second bullet on this slide highlights FDA's commitment to work with industry to develop a transitional In Vitro Diagnostic's approach to the regulation of emerging diagnostics.

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Leading up to the MDUFA III negotiations, FDA performed an analysis of the average time it took to clear a 510(k). The results of the analysis revealed several reasons which contributed to the changes in quantitative performance goals established in MDUFA III. These include:

- Two tier performance goals established in MDUFA II contributed to an overall increase in total time to a decision. Therefore, there is only one decision goal in MDUFA III, but other goals for milestones in the review process have been created. The other milestones include refuse to accept, substantive interactions and missed MDUFA goals.
- I have already discussed the Refuse To Accept and substantive interaction milestones in my previous slides but I have not addressed the missed MDUFA goal milestone. The missed MDUFA goal milestone was fondly nicknamed "No Submission Left Behind" during the negotiations. This milestone is intended to improve FDA transparency and accountability for those submissions which miss the target number of review days. To accomplish this, FDA will communicate with the applicant shortly after the decision goal is missed and discuss any outstanding issues with the applicant. FDA will also establish a timeline for making a MDUFA decision. This approach is intended to reduce the average overall time it takes to make a MDUFA decision.

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This table is a comprehensive list of all the performance goals outlined in MDUFA III. In many cases the number of days to a MDUFA decision has not changed from the MDUFA II performance goals.

It is the percentage of submissions that have to achieve the decision goals that has changed. The performance goals slowly ramp up over MDUFA III to allow for new hires to be brought on board and trained during the first four years of MDUFA III.

I have highlighted the performance goals for Fiscal Year 13 because they are the goals FDA will first need to focus on. As you can see, there are no longer separate performance goals for expedited and non-expedited PMAs. The original PMA and panel track supplement goals are now divided into PMAs that go to panel and PMAs that do not go to panel. In addition, the established goals for substantive interaction and the shared outcome goal of average total time are listed in this table.

Lastly, but very importantly for my in vitro diagnostic colleagues, I would like to point out that there are new CLIA waiver performance goals that did not exist previously in MDUFA II.

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MDUFA III includes funding for improvements in the premarket review infrastructure. One of the specified improvements was to increase the scientific and regulatory review capacity. FDA hired 32 FTEs in FY12 and we're well on our way to hire 65 FTEs in FY13. 90 of the 97 FTEs allocated during these two years are designated for CDRH. The 32 hires in FY12 were allocated to the two premarket review offices to reduce the supervisor to employee ratio by hiring additional supervisors to support the premarket reorganization.

MDUFA III fees will support an additional 240 FTES over the 5 years of the commitment. This will rise the total staffing supported by device user fees to approximately 500 FTES.

These additional hires will be brought on board over the course of the first 4 years of MDUFA III. The intent is to slowly ramp up the number of FTEs to allow for adequate new employee training. The ramp up of hiring in MDUFA III is intended to mirror the ramp up of performance goals in MDUFA III.

MDUFA III also specifies using user fees to enhance premarket reviewer and manager training. These include:

- mandatory training for all managers on the skills necessary to be a successful manager,
- continuing to support a mandatory Reviewer Certification Program which combines required courses and auditing of work product, and
- conducting mandatory training for all premarket review staff on the new MDUFA III commitments

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FDA agreed to participate with the device industry in a comprehensive assessment of the process for the review of device applications as part of the MDUFA III commitment letter. The commitment is to conduct a comprehensive assessment of FDA premarket review processes for medical devices and to identify opportunities for improvements that will significantly impact the review of device premarket applications. The Primary objectives for phase one include:

- Identification of best practices and prioritization of process improvements for conducting predictable, efficient, and consistent premarket reviews that meet regulatory review standards
- In-depth analysis of the elements of the review process in order to identify best practices and opportunities for improvement, including root cause analysis of selected significant factors
- Assessment of resource allocation to premarket device reviews across FDA
- Development of implementation plans for selected recommendations
- Development of metrics to ensure successful implementation of recommendations and demonstrate achievement of expected results

The phase two objective is to evaluate the implementation of selected recommendations.

In addition, FDA has committed to continue to meet with industry on a quarterly basis. The new reporting commitments in MDUFA III will provide more granular data consistent with FDA's efforts to be more transparent and accountable. These reports are available on FDA's webpage.

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Legislative language was also provided in FDAuSIA which supports MDUFA III.

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In previous years, certain kinds of medical device establishments required to register with the Agency, including initial importers, were exempted from paying the registration fee. As part of MDUFA III negotiations, all establishments required to register are now also required to pay the annual registration fee. The increase in establishments required to pay a registration fee allows for a more stable source of funding supporting the premarket review process.

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In FDAuSIA, congress granted explicit statutory authorization to FDA to implement the eCopy program for medical devices after an eCopy guidance document is finalized. The eCopy guidance describes how the FDA plans to implement the eCopy program. The inclusion of an eCopy is expected to improve the efficiency of the review process by allowing for immediate availability of an electronic version for review rather than relying solely on a paper version. The draft eCopy guidance document is currently available on FDA's webpage.

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The implementation of the new MDUFA III commitments required the collaboration of various parts of the agency to work together simultaneously. As you will see in the upcoming slides, the various parts of the agency are working like a well-oiled machine.

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The center has already pre-hired 32 new employees using reserved MDUFA II funding. These new hires are now working at CDRH and have filled the newly created manager positions in the ODE and OIVD reorganization. CDRH will also be advertising and interviewing in the coming weeks for current vacancies in the divisions and branches. In addition, FDA has also hired a "substantial" number of the 65 allotted full-time equivalent employees allocated as part of the MDUFA III funding for fiscal year 2013.

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There are three specific MDUFA III Guidance documents that are required in the commitment letter to be issued prior to implementation. I have listed them on this slide. All of these guidance documents have been issued as a draft document and included a comment period. They are:

- refuse to accept policy for 510(k)s

- acceptance and filing review for premarket approval applications, and
- the eCopy program for medical device submissions.

These documents can be found on FDA's webpage.

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The comment period for these draft documents has now closed. In order to facilitate an orderly commencement of the new policies outlined in these guidance documents, the new policies will be in effect starting Jan. 1, 2013 even if the guidance documents are finalized prior to Jan. 1st, 2013.

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There are several additional MDUFA III guidance documents which have been or will be issued. They include:

- Draft Guidance on Pre- Submission Interactions,
- Draft Guidance on Types of Communication During the Review of Medical Device Submissions. When final this guidance will supersede the Guidance for Industry and FDA Staff on Interactions During Review of Medical Device Submissions,
- Guidance for FDA and Industry regarding Actions on 510(k)s and the Effect on the Review Clock
- Guidance for FDA and Industry regarding Actions on PMAs and the Effect on the Review Clock
- Guidance on User Fees and Refunds for 510(k)s; and
- Guidance on User Fees and Refunds for PMAs

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In September of 2012 sixteen hours of mandatory MDUFA III training was required for all review staff. This training included an introduction to MDUFA III, the new performance goals and milestones for 510(k)s and PMAs, updated pre-submission interactions, updates to our electronic workload management tools, and the new goals for waivers submitted in accordance with the Clinical Laboratory Improvement Amendments. This training was recorded and is available to any reviewer who has been recently hired or who was unable to attend the training in September.

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During the transition period between October 1st and December 31st 2012 I encourage you to begin filling out the draft Refuse To Accept checklists to become more familiar with the required elements of a 510(k) and PMA. In addition, I strongly encourage you to include page numbers of where each element on the checklist is located and submit the checklist with your application. This will assist you in ensuring all elements of your application have been included and assist the reviewer in locating each of these elements during their refuse to accept review.

I also recommend that if you are submitting an application during the transition period you submit an eCopy along with it. This way we will have the opportunity to inform you if your eCopy was formatted properly or not. If your eCopy did not meet the technical specifications required for eCopy you will receive a report indicating why your eCopy did not meet the technical specifications. This way you will have the opportunity to test your eCopy prior to the requirement becoming effective.

To assist you with the eCopy requirement, FDA has created an eSubmitter tool which will assist you in creating your eCopy. This tool is available on FDA's webpage. Please note, this tool assists with the creation of an eCopy. It does not validate previously created eCopies, nor does it submit the application to FDA. You will need to send the eCopy created by the eSubmitter to FDA along with the required paper copies.

Lastly, in concert with the expanded pre-IDE program, we have also begun labeling pre-submissions with the letter "Q" instead of the letter "I" to assist the agency with the tracking and reporting of pre-submissions.

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As I previously mentioned, an Independent Assessment of CDRH's pre-market Review Process Management will be conducted. Phase I of the assessment is scheduled to begin in the spring of 2013. High priority recommendations are expected to be published six months after the contract is awarded and the assessment is expected to be completed in the spring of 2014 with implementation plans published 6 months after the receipt of each set of recommendations. Phase II of the implementation plan will be conducted to assess the effectiveness of the phase I recommendations. Phase II will begin in 2015 and be completed in 2016.

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One of the many efficiencies we have implemented is the generation of auto-e-mails in lieu of manually-generated correspondence. You should be on the lookout for these e-mails. They include acceptance review decisions, filing decision, substantive interaction decisions, and any missed MDUFA communication. Please note, not filing letters for PMAs and substantive interaction decisions other than to proceed interactively will still be sent through the mail. We hope that you will find this new method of communicating effective.

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Next, I would like to spend a few minutes explaining the difference between the terms interactive review and substantive interaction. A substantive interaction is an interim decision point for specific MDUFA III submissions, where interactive review is a process for requesting additional information from the sponsor while the submission is under review. A substantive interaction will either state that a file is being placed on hold, or a file is not going to be placed on hold and reviewed interactively.

The decision to proceed interactively or put the submission on hold will be made by the branch chief of the reviewing branch and it will be communicated to the applicant either electronically or by hard copy. If a decision is made to proceed interactively with the review of the application, the review clock will not be stopped for the remainder of the review process.

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Once a reviewer has communicated to you that they will proceed with an interactive review, the review clock does not stop. Therefore, it is very important for you to be responsive to the reviewer's requests. Some other policies regarding interactive review include that an interactive review is discretionary before the substantive interaction.

But it is required after FDA's request for additional information, or after stating we will proceed interactively. The guidance document I mentioned previously about the types of communication during the review of submissions will provide additional clarification regarding interactive review. Lastly, I would like to point out that almost all interactive review responses can be accepted through e-mail and added to the official review record so there is no need to follow-up with sending a hard copy to the document control center.

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You may be wondering? "Why is it that we no longer need to follow-up with a hard copy of information that we send in electronically?" The answer is "DocMan". Doc Man is short for CDRH's NEW Document Manager. It is an electronic repository that will be used to manage FDA's review records.

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You will now be able to e-mail your interactive review responses directly to DocMan instead of sending them to the document control center. We have assigned a unique e-mail address to DocMan. It is your document number @ docs.fda.gov. However, at the present time you can only e-mail DocMan during interactive reviews. If you are responding to a hold letter, you need to send your response to the document control center in order to restart the review clock. Some other benefits of DocMan include no longer printing all review correspondence documentation because we can transfer our files to our permanent archive system electronically, some correspondence such as refuse to accept decisions can be sent electronically, and best of all, it facilitates the use of digital signatures.

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Digital signatures allow for correspondence to be digitally signed and electronically dated. We are currently in the process of transitioning to digital signatures on all of our premarket review correspondence, regardless of whether we are sending the correspondence electronically or not. On this slide, the digital signature and electronic date are shown in the red boxes.

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At the present time, it is too early in the fiscal year to have any MDUFA III data to report on how we are performing, so I am going to show you an inspirational video instead. This is a middle school football game. The player in the red circle is my son.

You can always tell who he is because he has yellow cleats, yellow gloves, and a yellow, long sleeve shirt. It has been a long losing season for his team. They were playing the only team they thought they could beat in the league. My son went into this game determined to score a touchdown and this is what happened.

If we all work together, we, too, can score our very own MDUFA III touchdown.

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That's it for now. Thank you for taking the time to listen to this presentation. Should you need any additional information on MDUFA III, I have listed two FDA webpages as resources for you.

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